UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/540,443	06/22/2005	Robin L Polt	920214.00005	1404

26735 7590 05/07/2008

QUARLES & BRADY LLP
33 E. MAIN ST, SUITE 900
P.O BOX 2113
MADISON, WI 53701-2113

EXAMINER	
GROSS, CHRISTOPHER M	
ART UNIT	PAPER NUMBER
1639	

MAIL DATE	DELIVERY MODE
05/07/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/540,443	POLT ET AL.	
	Examiner	Art Unit	
	CHRISTOPHER M. GROSS	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 March 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4 and 7-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,7-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Responsive to communications entered 3/8/2007, 10/29/2007 and 3/7/2008. Claims 1,3,4,7-10 are pending. Claims 1,3,4,7-10 are under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Priority

This application is a 371 of PCT/US04/05340 tiled 02/24/2004 which claims benefit of provisional application 60/449,989 filed 02/25/2003 (referred to as '989).

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of '989, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. First, '989 does not disclose YtGFLS(beta-melibiose)-$CONH_2$, as set forth in claims 1,3,4,7, and 8. Second, '989 does not disclose peptide enkephalins *comprising* a formula YtGFLS(beta-disaccharide)$CONH_2$, which is open to other residues at the N

terminus as well as virtually any other chemical conjugate. See also 35 USC 112 first paragraph considerations concerning "new matter" below.

Therefore 2/24/2004 is the date for the purposes of prior art concerning claims 1,3,4,7-10.

Election/Restrictions

Applicant's election "SEQ ID 25" for the species of disaccharide glycosylated enkephalin with traverse in the reply filed on 10/29/2007 is acknowledged. Applicant's arguments are persuasive and the species are hereby rejoined.

Specification

The amendment filed 3/7/2008 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: The message sequence of the peptides in table 1 is no longer indicated by underlining.

Applicant is required to cancel the new matter in the reply to this Office Action.

Withdrawn Objection(s) and/or Rejection(s)

The rejection of claims 3,5-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is hereby withdrawn in view of applicant's amendments to the claims.

The rejection of claims 4-7 under 35 U.S.C. 102(b) as being anticipated by **Horvat et al** (1986 Synthesis 3:209-211 – IDS entry 9/26/2005) and evidenced by *Egelton et al* (2001 J. Pharmacology and Experimental Therapeutics 299:967-972 – IDS entry 9/26/2005) is hereby withdrawn in view of applicant's amendments to the claims.

The rejection of claims 1, 4-7 under 35 U.S.C. 102(b) as being anticipated by **Mitchell et al** (2001 JOC 66:2327-2342– IDS entry 9/26/2005) is hereby withdrawn in view of applicant's amendments to the claims.

The rejection of claims 1,4-5 and 7 under 35 U.S.C. 102(b) as being anticipated by **Elmagbari et al** (2001 FASEB Journal 15: p A915 Abstract – IDS entry 9/26/2005) is hereby withdrawn in view of applicant's amendments to the claims.

Maintained Claim Rejection(s) - 35 USC § 102

Claims 1,3,4,7 and 10 are rejected under 35 U.S.C. 102(a) as being anticipated by **Palian et al** (2003 JACS 125:5823-5831).

Response to Arguments

Applicant argues (i) Palian is not prior art; (ii) not all elements are taught.

Applicant's arguments have been fully considered but they are not deemed persuasive for the following reasons.

(i) Applicant argues, see p 12 third full paragraph of remarks entered 3/8/2007, that Palian et al being published electronically on 4/22/2003 does not represent prior art because the present application is afforded priority to 02/25/2003 through provisional application 60/449,989. It is noted, however for the reasons mentioned in the above

priority section, 2/24/2004 is the date for the purposes of prior art concerning claims 1,3,4,7-10, thus Palian et al represents pertinent prior art under 35 USC 102(a).

(ii) Applicant argues, see paragraph bridging pp 12-13 (3/8/2007), disaccharide containing glycopeptide 3 (YtGFLS(beta maltose)$CONH_2$) of Palian et al is not shown by to be *superior* to the monosaccharide containing glycopeptide 2 (YtGFLS(beta glucose)-$CONH_2$) of Palian et al with regard to Blood Brain Barrier (BBB) transport.

As mentioned in the last Office Action, Palian et al teach on page 5824, second paragraph glycosylation improves blood-brain barrier (BBB) penetration to produce potent analgesia in mice, thus the examiner submits, while monosaccharide containing peptides may require a greater amount than disaccharide containing peptides to achieve analgesia, Palian nevertheless teach the limitation of claim 1: "an effective amount of an analgesic molecule to be transported across a blood brain barrier," with regard to glycopeptides in general

Furthermore, in response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., disaccharide vs. monosaccharide superiority) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Notably claim 1 is drawn to an "effective amount..."

Further, in response to applicant's arguments, it is noted the recitations "to enable the peptide to be transported.." in claim 4 lines 1-2 and "capable of being

transported..." in claim 7 line 2 have not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

Lastly it should be noted, according to MPEP 2131.02, a species will anticipate a claim to a genus: "A generic claim cannot be allowed to an applicant if the prior art discloses a species falling within the claimed genus." In re Slayter, 276 F.2d 408, 411, 125 USPQ 345, 347 (CCPA 1960). Thus, said beta-maltose glycopeptide 3 of Palian et al anticipates the species set forth in claim 10 as well as the genera set forth in claims 1,3,4,7.

Please note that the above rejection has been modified from the original version to more clearly address applicants' newly amended and/or added and/or cancelled claims.

Maintained Claim Rejection(s) - 35 USC § 103

Claims 1,3,4,7,8,9 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Roques et al** (US Patent 4,407,794 – IDS entry 9/26/2005) in view of **Mitchell et al** (2001 JOC 66:2327-2342– IDS entry 9/26/2005).

Response to Arguments

The declaration under 37 CFR 1.132 filed 3/8/2007 is insufficient to overcome the rejection of claims 1,3,4,7,8,9 based upon Roques et al in view of Mitchell et al under 35 USC 103 (a) as set forth in the last Office action because:

First applicant argues, see third full paragraph 13 of remarks entered 3/8/2007 and the declaration entered 3/8/2007 p 3 section 8, that the Roques patent does not disclose glycosylation of the parent peptide YtGFLS.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Here, glycosylation with lactose and melibiose are provided by Mitchell et al, see for instance compounds 14 and 16 in figure 3.

Second, applicant argues, see paragraph bridging pp 13-14 remarks entered 3/8/2007 and declaration entered 3/8/2007 p 3 section 9, that Mitchell does not disclose the parent peptide YtGFLS.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Here, parent peptide YtGFLS is provided by Roques et al, see for instance table 1 compound 4.

Third, applicant argues, see p 14 first full paragraph that the examiner is using "obvious to try" rationale, which, according to applicant, is not the standard of 35 USC 103.

In this regard, the Supreme Court has stated in KSR Int'l Co. v. Teleflex Inc No. 04-1350 (S.Ct. Apr 30, 2007) /550 U.S._____, 82 USPQ2d 1385 (2007) that a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious over section 103. See especially *KSR* U.S._____, 82 USPQ2d at 1397 (2007). Emphasis added.

In this light, the following findings of fact are presented: (i) a finding that at the time of the invention there had been a recognized problem or need in the art, including a design need or market pressure to solve a problem; (ii) a finding that there had been a finite number of identified, predictable potential solutions to the recognized need or problem; (iii) a finding that one of ordinary skill in the art could have pursued the known potential solution with a reasonable expectation of success.

(i) Mitchell et al mention on p 2328 first full paragraph, "Peptides have been discounted as drug candidates due to a perceived instability to hydrolytic enzymes...and due to the blood-brain brain barrier (BBB), which blocks their entry into the central nervous system." The examiner submits therefore that the problem of peptides as drug candidates had been recognized at the time the invention was made. In fact, applicant admits so much on p 3 section 8, lines 5-6 of the declaration stating that the peptides of

Roques have no utility as pharmaceuticals due to their poor biodistribution and inability to penetrate the BBB.

(ii) Applicant admits on p 3 section 8, lines 4-5 of the declaration that Roques' compounds are *common* enkephalin analogues.

In an effort toward achieving better biodistribution and BBB penetration of enkephalin analogs, Mitchell et al disclose a series of monosaccharide and disaccharide glycoside amino acid derivatives used in preparing glycopeptides, such as shown in figure 6. The examiner submits that the monosaccharide and disaccharide glycoside amino acid derivatives of Mitchell et al represent a finite number of identified, predictable potential solutions to the recognized need for providing better BBB transport and biodistribution of peptides drug candidates, including the art-recognized (common) enkephalin analogues of Roques et al.

(iii) One of ordinary skill in the art could incorporate the monosaccharide and disaccharide glycoside amino acid derivatives into the peptides of Roques et al with a reasonable expectation of success since Mitchell et al state "Glycosylation has been used as a method to penetrate the BBB, and enkephalin analogues glycosylated at or near the C-terminus were shown to elicit prolonged and profound analgesia in mice. Similar results have been obtained with glycosylated vasopressin analogues and with deltorphin and dermorphin glycopeptide analogues."

Fourth, applicant argues, see second full paragraph p 14 of remarks entered 3/8/2007 that the examiner is using impermissible hindsight to reject the claims.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

The motivation to incorporate the monosaccharide and disaccharide glycoside amino acid derivatives of Mitchell et al into the parent enkephalin peptides of Roques et al concerns providing a means of penetrating the BBB resulting in prolonged analgesia is taken from Mitchell et al on p 2328 first full paragraph and *not* taken from instant specification.

Please note that the above rejection has been modified from the original version to more clearly address applicants' newly amended and/or added and/or cancelled claims.

New Claim Rejections - 35 USC § 112

The following is a quotation of the **second** paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7,8,9,10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

This rejection is necessitated by Applicant's amendment to the claims.

Claim 7 recites the limitation "the disaccharide" in line 4. There is insufficient antecedent basis for this limitation in the claim. It should probably read the β-disaccharide.

Unlike claims 1,3, and 4 which recite β-disaccharide, indicating the beta anomer, claims 7,8,9 and 10 each recite vague and indefinite language in β-lactose, β-maltose and β-melibose, which to one of skill in the art may indicate the glycosyl portion is in a beta anomeric configuration, or alternatively indicate the disaccharides lactose maltose and melibiose are merely connected to the beta carbon of Serine in either anomeric configuration alpha or beta.

New Claim Rejection(s) – 35 USC § 112

The following is a quotation of the **first** paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1,4,7-10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection is necessitated by Applicant's amendment to the claims.

Claims 1,7-10 have been amended to recite peptide enkephalins *comprising* a formula YtGFLS(beta-disaccharide)$CONH_2$, which is open to other residues at the N terminus as well as virtually any other chemical conjugate. Claim 4 has been amended to peptide enkephalins *having* a formula YtGFLS(beta-disaccharide)$CONH_2$, which is similarly open to other residues at the N terminus as well as virtually any other chemical conjugate.

The specification as originally filed provided no implicit or explicit support for peptide enkephalins bearing chemical modifications on the "message" portion of the sequence.

Applicants are reminded that it is their burden to show where the specification supports any amendments to the disclosure. See MPEP 714.02, paragraph 5, last sentence and also MPEP 2163.06 I.

MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition

to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP 2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. *Applicant should therefore specifically point out the support for any amendments made to the disclosure.*

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher M. Gross whose telephone number is (571)272-4446. The examiner can normally be reached on M-F 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, J. Douglas Schultz can be reached on 571 272-0763. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Christopher M Gross
Examiner
Art Unit 1639

cg

/Mark L. Shibuya, Ph.D./
Primary Examiner, Art Unit 1639